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DATE: Friday, July 23, 2004

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☐	L9	9200388	1
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L12: Entry 9 of 22 File: USPT Jun 10, 2003

DOCUMENT-IDENTIFIER: US 6576478 B1
** See image for Certificate of Correction **
TITLE: Microdevices for high-throughput screening of biomolecules

Detailed Description Text (101):
A wide range of detection methods are applicable to this and other methods of the invention. The invention device can be interfaced with a means for detection of absorption in the visible range, chemiluminescence, or fluorescence (including lifetime, polarization, fluorescence correlation spectroscopy (FCS), and fluorescence-resonance energy transfer (FRET)). Furthermore, built-in detectors such as optical waveguides (PCT Publication WO 96/26432 and U.S. Pat. No. 5,677,196), surface plasmons, and surface charge sensors are compatible with many embodiments of the invention.

Detailed Description Text (147):
HIV protease requires at least a heptapeptide substrate (Moore et al., Biochem. Biophys. Res. Commun., 1989, 159:420). To analyze the activity of the different HIV variants, a continuous assay based on intra-molecular fluorescence resonance energy transfer (FRET) is used. A peptide substrate corresponding to the p17-p24 cleavage site of the viral gag protein (Skalka, Cell, 1989, 56:911) is modified by the addition of an energy-transfer pair (Geoghegan et al., FEBS Lett., 1990, 261:119): In Dns-Ser-Gln-Asn-Tyr-Pro-Ile-Val-Trp (Dns-SONYPIVW; SEQ ID NO:3), the Dns (dansyl) and Trp groups are the N- and C-terminal extensions, respectively. (Geoghegan et al.). Excitation of Trp is at 290 nm, and emission of Dns is at 575 nm. Cleavage of the peptide at the Tyr-Pro bond reduces the Dns emission and increases Trp emission at 360 nm. The modified heptapeptide Dns-SONYPIVW is prepared as described (Geoghegan et al.) and analyzed by amino acid analysis, nuclear magnetic resonance and mass spectrometry. The purity is checked by HPLC analysis using a Vydac C-4 column and an acetonitrile gradient in 0.1% TFA. In order to test the activity of all the HIV variants described above, each microchannel with an immobilized HIV variant (see Example 6) is filled with 20 .mu.M of Dns-SQNYPIVW in 50 mM sodium acetate, pH 5.5, 13% glycerol, 10 mM DTT. Addition of the substrate to the immobilized proteins leads to time-dependent intensity changes in the fluorescence emission spectrum. The 360 nm Trp emission peak progressively will increase to about 2.5 times its initial intensity, while the Dns group's emission band (575 mm) will decline in intensity. This intensity change will be observed in all the channels containing active forms of the HIV variants. To control for changes in background fluorescence, GST-K.sub.6 fusion protein is measured in parallel.

CLAIMS:

1. A multi-channel sample detection device, comprising (a) a substrate having an upper surface, (b) a plurality of discrete open channels formed in or on said substrate adjacent said upper surface, each channel extending between first and second ends and having a bottom wall surface defining an immobilization region intermediate said first and second ends, (c) a cover attached to said substrate's upper surface and forming with each channel a closed channel having open first and second ends, said cover being part of a detection system for detecting interactions within each channel, where said first ends of said channels arranged so that said

channels can each be both independently loaded with an analyte containing fluid, or simultaneously loaded with said fluid by loading said channels simultaneously with a a bulk-loading dispenser device, (d) a plurality of immobilization molecules for immobilizing selected proteins or peptides or small molecules or nucleic acids, said said immobilization molecules being chemisorbed or physisorbed to said immobilization region in each channel, wherein when said liquid containing said one or more analytes is introduced into said channels to interact with said peptides or proteins or small molecules or nucleic acids, such interactions, if any, can be detected by said detection device.